REMARKS

Status of the Claims

Pending claims

Claims 93 to 119 are pending.

Claims amended and added in the instant amendment

In the present response, claims 93 to 119 are amended, and new claims 120 to 137 are added. Accordingly, after entry of the instant amendment, claims 93 to 137 will be pending and under examination.

Outstanding Rejections

Claims 94, 105 to 115, 118 to 119 are rejected under 35 U.S.C. §112, second paragraph. Claims 93 to 103 and 105 to 119 are rejected under 35 U.S.C. §112, first paragraph. Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

Claim 104 Allowable

Applicants thank the Examiner for finding claim 104 allowable.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. Support for claims directed to methods for making a polypeptide using a nucleic acid of the invention can be found, *inter alia*, on page 21, line 25 to page 25.

Information Disclosure Statement

Applicants thank the Examiner for expressly considering (and initialing) the submitted Information Disclosure Statements (IDSs) and Forms PTO-1449.

Priority

As requested by the Examiner, to clarify the status of the sequences, Applicants note that no amino acid changes resulted from re-sequencing of the plasmid 18GC.

Drawings

The attached sheet of drawings includes changes to Figure 5A. This sheet replaces the original sheet of Figure 5A. In the corrected Figure 5A the codon TTG is correctly indicated as encoding Leucine (Leu). An annotated sheet showing changes is also attached.

Issues under 35 U.S.C. §112, second paragraph

Claims 94, 105 to 115, 118 to 119 stand rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The term "about"

The Patent Office alleged claim 94 is indefinite because of the term "about" (see paragraph 8, page 4, of the office action). Applicants respectfully traverse. In Ecolab, Inc. v. Envirochem, Inc., 60 USPQ 2d 1173 (Fed. Cir. 2001), 264 F.3d 1358, the Federal Circuit stated that the terms "about" and "substantially" are descriptive terms commonly used in patent claims to "avoid a strict numerical boundary to the specified parameter." Pall Corp. v. Micron Seps., 66 F.3d 1211, 1217, 36 USPQ2d 1225, 1229 (Fed. Cir. 1995); See, e.g., Andrew Corp. v. Gabriel Elecs. Inc., 847 F.2d 819, 821-22, 6 USPQ2d 2010, 2013 (Fed. Cir. 1988) (noting that terms such as "approach each other," "close to," "substantially equal," and "closely approximate" are ubiquitously used in patent claims and that such usages, when serving reasonably to describe the claimed subject matter to those of skill in the field of the invention, and to distinguish the claimed subject matter from the prior art, have been accepted in patent examination and upheld by the courts).

The phrase "the purified polypeptide"

Claim 94 is alleged to be indefinite because of the phrase "the purified polypeptide." The instant amendment addresses the Examiner's concerns.

Issues under 35 U.S.C. §112, first paragraph

Written Description

Claims 105 to 115 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the art that the inventors at the time the application was filed had possession of the claimed invention.

Applicants thank the Examiner for acknowledging that (1) the instant claims now recite a specific function for the claimed polypeptides, (2) a test for activity is provided in the application, (3) assessing percent homology is well known in the art; and, (4) a skilled artisan is well-versed in protocols used for biological research. The Patent Office also notes that a genus of polypeptides can be achieved by a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus.

However, the Patent Office alleges that the recited structural features of the claimed genus does not constitute a substantial portion of the genus because (1) the remainder of the structure of the claimed polypeptide is undefined, and, (2) the specification does not provide the remaining structural features necessary for members of the genus to be selected (see page 6, lines 5 to 9, of the instant office action).

After entry of the instant amendment, claims 105 to 115 are drawn to isolated or recombinant polypeptides comprising at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 100 or 150 consecutive amino acids of the polypeptide of claim 93 or claim 104 and having alpha-galactosidase activity. Thus, claims 105 to 115 are drawn to active fragments of a polypeptide of the invention (a polypeptide of claim 93 or claim 104).

Applicants respectfully maintain that only the claimed sequence need be described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors at the time the application was filed had possession of the claimed invention to satisfy the requirement of the written description requirement of section 112, first paragraph. The claimed polypeptides can have additional sequence because of use of open, or "comprising", language. However, these additional structural features, if any, need not be described in the specification.

Applicants respectfully submit that the claimed invention is sufficiently described in the specification such that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing.

Applicants respectfully refer to the USPTO guidelines concerning compliance with the written description requirement of U.S.C. §112, first paragraph. In example 14 of the guidelines (a copy of which is attached as Exhibit A), a claim reciting variants claimed by sequence identity to a sequence is sought (specifically, "A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B). In the example, the specification is described as providing SEQ ID NO:3 and a function for the protein. The specification contemplates, but does not exemplify variants of SEQ ID NO:3 that can have substitutions, deletions, insertions and additions. Procedures for making proteins with substitutions, deletions, insertions, and additions are routine in the art and an assay is described which will identify other proteins having the claimed catalytic activity. The analysis of example 14 states that procedures for making variants (which have 95% sequence identity) are conventional in the art. The Guidelines conclusion states that the disclosure meets the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention. The USPTO guidelines recognize that the written description requirement is met for a genus of polypeptides described by structure, a physico-chemical property (e.g., a % sequence identity, stringent hybridization) and a defined function. Accordingly, the genus of claimed polypeptides also meet the written description requirements of section 112.

Analogously, the polypeptides of the claim invention are described by structure (the exemplary polypeptide sequences), a physico-chemical property (percent sequence identity) and function (alpha galactosidase activity). All polypeptides of the claimed genus must have at least about 50% sequence identity to a subsequence of SEQ ID NO:4, the exemplary alpha galactosidase, and must have alpha galactosidase activity.

Furthermore, the claims fully comply with the requirements for written description of a genus of nucleic acids as set forth in University of California v. Eli Lilly & Co., 43 USPQ2d 1398 (Fed. Cir. 1997). In Lilly, the Court stated that, "[a] description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs....*or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.*" (emphasis added) Lilly, 43USPQ2d at 1406.

As noted above, the instant claims clearly set forth specific structural and physical characteristics of the claimed alpha galactosidases. The claimed genus of polypeptides must

have alpha galactosidase activity and a specific physical characteristic, e.g., a % sequence identity to the exemplary SEQ ID NO:4. Therefore, the claimed sequences are defined via shared physical and structural properties in terms that "convey with reasonable clarity to those skilled in the art that Applicant, as of filing date sought, was in possession of invention." (Vas-Cath Inc. V. Mahukar, 19 USPQ2d 1111, (Fed Cir. 1991)).

More recently, the Federal Circuit stated

Similarly, in this court's most recent pronouncement, it noted:

> More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.

Amgen, 314 F.3d at 1332 [Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1330, 65 USPQ2d 1385, 1397 (Fed. Cir. 2003)].

Moba, B.V. v. Diamond Automation, Inc., 2003 U.S. App. LEXIS 6285; Fed. Cir. 01-1063, -1083, April 1, 2003.

Analogously, the disclosed function of the alpha galactosidases of the instant invention is sufficiently correlated to a particular, known structure (the exemplary sequences) and a physical (physico-chemical) property (percent sequence identity). Accordingly, the sequences used in the claimed methods are defined via shared physical and structural properties (and function - alpha galactosidase activity) in terms that convey with reasonable clarity to those skilled in the art that Applicants, as of the filing date and at the time of the invention, were in possession of the claimed invention.

Enablement

Claims 93 to 103 and 105 to 119 are rejected under 35 U.S.C. §112, first paragraph, as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention.

The Patent Office states that the specification is enabling for the polypeptide of SEQ ID NO:4.

However, the Patent Office alleges, inter alia, that the specification is not enabling for a polypeptide having 50% to 95% sequence identity to SEQ ID NO:4, or any polypeptide

comprising at least 10 to 150 consecutive amino acids of the polypeptide of SEQ ID NO:4. It is alleged that it would require undue experimentation for one skilled in the art to arrive at the genus of claimed polypeptides. In particular, it is alleged that it is not routine experimentation to randomly create an infinite number of variants and test them for activity, and that it would have required some knowledge or guidance as to which are the structural elements (amino acid residues) which correlate with alpha galactosidase activity before creating variants and testing them for activity.

Applicants respectfully maintain that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, a genus of alpha galactosidases of the invention. As declared by Dr. Jay Short (see attached Rule 132 declaration), the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art, e.g., screening enzymes, and nucleic acids encoding enzymes, for alpha galactosidase activity, was very high. As declared by Dr. Short, using the teaching of the specification, including the glycosidase activity assay set forth in Example 2, pages 71 to 72 of the specification, one skilled in the art could have selected routine methods known in the art at the time of the invention to express variants of nucleic acids encoding the exemplary enzyme of the invention and screen them for expression of polypeptides having alpha galactosidase activity. Dr. Short declares that one skilled in the art could have used routine protocols known in the art at the time of the invention, including those described in the instant specification, to screen for polypeptides having 50% sequence identity to SEQ ID NO:4, or active fragments thereof, for alpha galactosidase activity. As declared by Dr. Short, while the numbers of samples needed to be screened may have been high, the screening procedures were routine and successful results (i.e., finding variant alpha galactosidases and/or active fragments thereof) predictable. Furthermore, Dr. Short declares that it would not have required any knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues, that correlate with alpha galactosidase activity to create variants of the exemplary polypeptide and test them for alpha galactosidase activity, or to create variants of nucleic acids encoding the exemplary polypeptides and test them for the expression of polypeptides having alpha galactosidase activity. Accordingly, it would not have taken undue experimentation to make and use the claimed invention, including

identification of a genus of alpha galactosidases, or, a genus of nucleic acids encoding alpha galactosidases.

Whether large numbers of compositions (e.g., enzymes, antibodies, nucleic acids, and the like) must be screened to determine if one is within the scope of the claimed invention is irrelevant to an enablement inquiry. Enablement is not precluded by the necessity to screen large numbers of compositions, as long as that screening is "routine," i.e., not "undue," to use the words of the Federal Circuit. The Federal Circuit in In re Wands directed that the focus of the enablement inquiry should be whether the experimentation needed to practice the invention is or is not "undue" experimentation. The court set forth specific factors to be considered.

One of these factors is "the quantity of experimentation necessary." Guidance as to how much experimentation may be needed and still not be "undue" was set forth by the Federal Circuit in, e.g. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). In Hybritech, Inc., a single deposited antibody producing cell line enabled a claim generic to all IgM antibodies directed to a specific antigen. The Federal Circuit noted that the evidence indicated that those skilled in the monoclonal antibody art could, using the state of the art and applicants' written disclosure, produce and screen new hybridomas secreting other monoclonal antibodies falling within the genus without undue experimentation. The court held that applicants' claims need not be limited to the specific, single antibody secreted by the deposited hybridoma cell line (significantly, the genus of antibodies was allowed even though only one antibody specie was disclosed). The court was acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."

Analogously, practitioners of the biological sciences for the instant invention also recognize the need to screen numbers of negatives to find a sample that has the desired properties, e.g., polypeptides having alpha galactosidase activity. Furthermore, as declared by Dr. Short, the screening procedures used to identify polypeptides within the scope of the instant invention, or nucleic acids encoding alpha galactosidases, were all well known in the art and at the time this application was filed. All were routine protocols for the skilled artisan. Thus, the

skilled artisan using Applicants' written disclosure could practice the instant claimed invention without undue experimentation.

Enablement is not precluded by the necessity to screen large numbers of alternative compounds (e.g., nucleic acids or polypeptides), as long as that screening is "routine," i.e., not "undue." As declared by Dr. Short, it would have taken only routine protocols to make variants of the exemplary polypeptides of the invention, or the nucleic acids encoding them, and screen them to identify polypeptides with alpha galactosidase activity, or, nucleic acids encoding polypeptides with alpha galactosidase activity. Thus, the specification enabled the skilled artisan at the time of the invention to make and use a broad genus of alpha galactosidase.

CONCLUSION

In view of the foregoing amendment and remarks, it is believed that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs. Applicants believe all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present response and amendment. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050. Please credit any overpayment to this account.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (858) 678-5070.

Respectfully submitted,

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